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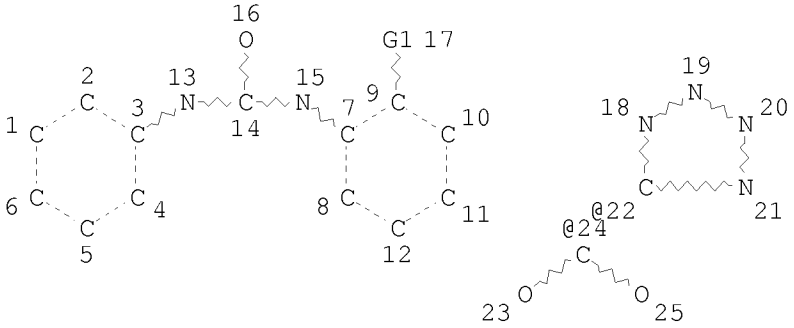
L1 HAS NO ANSWERS
L1 STR



VAR G1=22/24
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 8 3
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

=> d his l3

(FILE 'REGISTRY' ENTERED AT 08:27:20 ON 17 SEP 2008)
L3 1253 S L1 FUL

=> d his l4

(FILE 'REGISTRY' ENTERED AT 08:27:20 ON 17 SEP 2008)
L4 244 S L3 AND TETRAZO?

=> d his l5

(FILE 'CAPLUS' ENTERED AT 08:32:24 ON 17 SEP 2008)
L5 18 S L4

=> d his l6

(FILE 'CAPLUS' ENTERED AT 08:32:24 ON 17 SEP 2008)
L6 6 S L5 AND (CHLORID?(5A)CHANNEL?)

FILE 'REGISTRY' ENTERED AT 08:35:17 ON 17 SEP 2008

=> d bib abs 1-6
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L6 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:1127351 CAPLUS
DN 142:56011

TI Preparation of diphenylurea derivatives and their use as chloride channel blockers
IN Dahl, Bjarne H.; Christophersen, Palle
PA Neurosearch A/S, Den.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004111017	A1	20041223	WO 2004-EP51111	20040615
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004247429	A1	20041223	AU 2004-247429	20040615
	CA 2529806	A1	20041223	CA 2004-2529806	20040615
	EP 1638948	A1	20060329	EP 2004-741799	20040615
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
	BR 2004010576	A	20060620	BR 2004-10576	20040615
	CN 1805942	A	20060719	CN 2004-80016868	20040615
	JP 2006527735	T	20061207	JP 2006-516151	20040615
	MX 2005PA13269	A	20060317	MX 2005-PA13269	20051207
	IN 2005CN03416	A	20070223	IN 2005-CN3416	20051215
	US 20060178413	A1	20060810	US 2005-561189	20051216
	NO 2006000231	A	20060116	NO 2006-231	20060116
PRAI	DK 2003-898	A	20030617		
	WO 2004-EP51111	W	20040615		

OS MARPAT 142:56011
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein Ro, Rm, Rp = independently H, halo, CF3, OCF3, alkyl, alkoxy; with the proviso that not all three of Ro, Rm, Rp = H; R2, R3, R4, R5 = independently H, halo, CF3, OCF3, alkyl, alkoxy; with the absence of 1-(3-trifluoromethylphenyl)-3-[3-(1H-tetrazol-5-yl)-4'-trifluoromethylbiphenyl-4-yl]urea; and their pharmaceutically acceptable salts] were prepared for use as chloride channel blockers in the treatment of bone metabolic diseases, or diseases responsive to inhibition of angiogenesis (no data). For example, II was prepared in 3 steps by coupling of 2-amino-5-bromobenzonitrile with [4-(trifluoromethyl)phenyl]boronic acid, cyclization with sodium azide, and reaction of biphenylamine with 4-chloro-3-trifluoromethylphenyl isocyanate.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:591850 CAPLUS
DN 142:49140
TI The chloride channel inhibitor N53736 prevents bone resorption in ovariectomized rats without changing bone formation
AU Schaller, Sophie; Henriksen, Kim; Sveigaard, Christina; Heegaard, Anne-Marie; Helix, Nathalie; Stahlhut, Martin; Ovejero, Maria C.; Johansen, Jens V.; Solberg, Helene; Andersen, Thomas L.; Hougaard, Dorit; Berryman, Mark; Shiodt, Christine B.; Sorensen, Bjorn H.; Lichtenberg, Jens; Christophersen, Palle; Foged, Niels T.; Delaisse, Jean-Marie; Engsig, Michael T.; Karsdal, Morten A.
CS Nordic Bioscience A/S, Herlev, Den.
SO Journal of Bone and Mineral Research (2004), 19(7), 1144-1153
CODEN: JBMREJ; ISSN: 0884-0431
PB American Society for Bone and Mineral Research
DT Journal
LA English
AB Chloride channel activity is essential for osteoclast function. Consequently, inhibition of the osteoclastic chloride channel should prevent bone resorption. Accordingly, we tested a chloride channel inhibitor on bone turnover and found that it inhibits bone resorption without affecting bone formation. This study indicates that chloride channel inhibitors are highly promising for treatment of osteoporosis. Introduction: The chloride channel inhibitor, NS3736, blocked osteoclastic acidification and resorption in vitro with an IC50 value of 30 μM. When tested in the rat ovariectomy model for osteoporosis, daily treatment with 30 mg/kg orally protected bone strength and BMD by .apprx.50% 6 wk after surgery. Most interestingly, bone formation assessed by osteocalcin, mineral apposition rate, and mineralized surface index was not inhibited. Materials and Methods: Anal. of chloride channels in human osteoclasts revealed that C1C-7 and CLIC1 were highly expressed. Furthermore, by electrophysiol., we detected a volume-activated anion channel on human osteoclasts. Screening 50 different human tissues showed a broad expression for CLIC1 and a restricted immunoreactivity for C1C-7, appearing mainly in osteoclasts, ovaries, appendix, and Purkinje cells. This highly selective distribution predicts that inhibition of C1C-7 should specifically target osteoclasts in vivo. We suggest that NS3736 is inhibiting C1C-7, leading to a bone-specific effect in vivo. Results and Conclusion: In conclusion, we show for the first time that chloride channel inhibitors can be used for prevention of ovariectomy-induced bone loss without impeding bone formation. We speculate that the coupling of bone resorption to bone formation is linked to the acidification of the resorption lacunae, thereby enabling compds. that directly interfere with this process to be able to pos. uncouple this process resulting in a net bone gain.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:220307 CAPLUS
DN 140:270555
TI Preparation of diarylurea derivatives and their use as chloride channel blockers
IN Dahl, Bjarne H.; Christophersen, Palle; Engsig, Michael Thyrring; Karsdal, Morten Asser; Foged, Niels Taekker; Jensen, Flemming Reissig
PA Neurosearch A/s, Den.
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004022529	A2	20040318	WO 2003-DK575	20030904
	WO 2004022529	A3	20040513		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2495284	A1	20040318	CA 2003-2495284	20030904
	AU 2003258490	A1	20040329	AU 2003-258490	20030904
	EP 1537075	A2	20050608	EP 2003-793605	20030904
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	CN 1678573	A	20051005	CN 2003-820985	20030904
	JP 2005538152	T	20051215	JP 2004-533214	20030904
	NZ 538513	A	20070223	NZ 2003-538513	20030904
	MX 2005PA02493	A	20050527	MX 2005-PA2493	20050304
	US 20060160856	A1	20060720	US 2005-526208	20050916
PRAI	DK 2002-1306	A	20020905		
	DK 2002-1310	A	20020905		
	WO 2003-DK575	W	20030904		

OS MARPAT 140:270555

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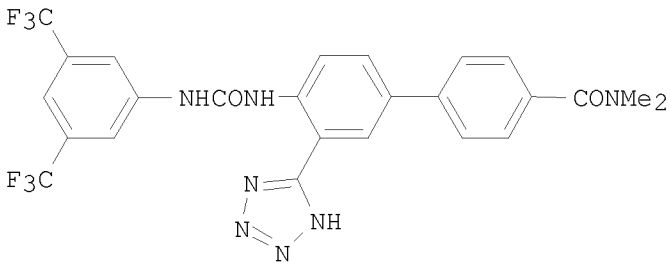

I

AB ANHCONR1D [A = (un)substituted cyclohexyl, Ph, pyridyl, thienyl, naphthyl, indolyl, pyrazolyl, oxopyrrolidinyl; R1 = H, D = (un)substituted Ph, cyclohexyl, 2-pyridinyl, CHR2CO2H; R2 = (un)substituted Ph; R1D = CH(CO2H)CH2CHR3CH2; R3 = H, OH] were prepared for use as chloride channel blockers in the treatment of bone metabolic diseases, diseases responsive to modulation of the mast cell or basophil activity, diseases responsive to inhibition of angiogenesis, or sickle cell anemia (no data). Thus, 4-BrC6H4Me was converted to 4-MeC6H4B(OH)2, which was oxidized to 4-HO2CC6H4B(OH)2 and amidated to 4-Me2NCOC6H4B(OH)2. Coupling with 5,2-Br(H2N)C6H3CN gave 4,3-H2N(NC)C6H3C6H4CONMe2-4 which was cyclized to the tetrazole and treated with 3,5-(F3C)2C6H3NCO to give the urea I.

L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:37988 CAPLUS
DN 140:368377
TI Inhibition of the Endogenous Volume-regulated Anion Channel (VRAC) in HEK293 Cells by Acidic Di-Aryl-Ureas
AU Helix, N.; Strobaek, D.; Dahl, B. H.; Christophersen, P.

CS NeuroSearch A/S, Ballerup, DK-2750, Den.
SO Journal of Membrane Biology (2003), 196(2), 83-94
CODEN: JMBBBO; ISSN: 0022-2631
PB Springer-Verlag New York Inc.
DT Journal
LA English
AB The endogenous volume-regulated anion channel (VRAC) from HEK293 cells was pharmacol. characterized using the whole-cell patch-clamp technique. Under isotonic conditions a small (1.3 nS), Ca2+-independent Cl conductance was measured. However, swelling at 75% tonicity activated a VRAC identified as an outward-rectifying anion current (PI > PCl > Pgluconate), which was ATP-dependent and showed inactivation at pos. potentials. Activation of this current followed a sigmoid time course, reaching a plateau conductance of 42.6 nS after 12-15 min (t1/2 = 7 min). The pharmacol. of this VRAC was investigated using standard Cl--channel blockers (NPPB, DIDS, and tamoxifen) as well as a new group (acidic di-aryl ureas) of Cl--channel blockers (NS1652, NS3623, NS3749, and NS3728). The acidic di-aryl ureas were originally synthesized for inhibition of the human erythrocyte Cl- conductance in vivo. NS3728 was the most potent VRAC blocker in this series (IC50 = 0.40 μM) and even more potent than tamoxifen (2.2 μM). NS3728 accelerated channel inactivation at pos. potentials. These results show that acidic di-aryl ureas constitute a promising starting point for the synthesis of potent inhibitors of VRAC.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:241346 CAPLUS
DN 136:279203
TI Substituted phenyl derivatives, their preparation and use
IN Dahl, Bjarne H.; Christophersen, Palle
PA Neurosearch A/S, Den.
SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 837,166.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20020037905	A1	20020328	US 2001-923458	20010808
	US 6696475	B2	20040224		
	CA 2285424	A1	19981029	CA 1998-2285424	19980421
	WO 9847879	A1	19981029	WO 1998-DK162	19980421
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9869196	A	19981113	AU 1998-69196	19980421
	AU 728520	B2	20010111		
	EP 977741	A1	20000209	EP 1998-914851	19980421
	EP 977741	B1	20030903		
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	TR 9902593	T2	20000321	TR 1999-2593	19980421
	BR 9808938	A	20000801	BR 1998-8938	19980421
	NZ 337976	A	20010525	NZ 1998-337976	19980421

PI JP 2001521532 T 20011106 JP 1998-544759 19980421
SK 282818 B6 20021203 SK 1999-1447 19980421
RU 2197482 C2 20030127 RU 1999-124188 19980421
CN 1118462 C 20030820 CN 1998-804446 19980421
AT 248824 T 20030915 AT 1998-914851 19980421
PT 977741 T 20040130 PT 1998-914851 19980421
ES 2205472 T3 20040501 ES 1998-914851 19980421
CZ 295822 B6 20051116 CZ 1999-3699 19980421
US 6297261 B1 20011002 US 1999-402165 19990930
WO 2000024707 A1 20000504 WO 1999-DK575 19991019
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
JP 2003246773 A 20030902 JP 2003-22576 19991019
EP 1514867 A2 20050316 EP 2004-105861 19991019
EP 1514867 A3 20050323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, MK, CY, AL
MX 9909689 A 20000331 MX 1999-9689 19991021
HK 1026909 A1 20040416 HK 2000-106125 20000927
US 20020032210 A1 20020314 US 2001-837166 20010419
US 6706749 B2 20040316
PRAI DK 1997-452 A 19970422
WO 1998-DK162 W 19980421
DK 1998-1362 A 19981022
US 1999-402165 A2 19990930
WO 1999-DK575 A1 19991019
US 2001-837166 A2 20010419
EP 1999-950505 A3 19991019
JP 2000-578279 A3 19991019
OS MARPAT 136:279203
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; 1 of R1-R3 = acidic functional group having pKa < 8 or a group convertible in vivo to such a group; R4, R5 and the others of R1-R3 = independently H, alkyl, alkoxy, OH, halo, CF3, cyano, NO2, amino, etc.; Y = C(X)NR0, NR0C(X)NR00, etc.; R0, R00 = independently H, alkyl; X = O, S; R11-R15 = independently H, alkyl, alkoxy, OH, halo, CF3, cyano (substituted) aryl, heteroaryl, phenylamino, etc.] were prepared Thus, 3-Trifluoromethylphenyl isocyanate and 2-aminobenzoic acid were stirred in PhMe to give N-3-trifluoromethylphenyl, N'-2-carboxyphenyl urea (II). The compds. are useful as chloride channel blockers. N-3-trifluoromethylphenyl-N'-[4'-(dimethylsulfamoyl)-2-(1H-tetrazol-5-yl)-4-biphenyl]urea (III) blocked erythrocyte chloride channels with KD = 0.3 μM.

L6 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:290984 CAPLUS
DN 132:308142
TI Preparation of diarylureas and related compounds as chloride channel blockers.

IN Dahl, Bjarne H.; Christophersen, Palle
PA Neurosearch A/s, Den.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000024707	A1	20000504	WO 1999-DK575	19991019
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2342626	A1	20000504	CA 1999-2342626	19991019
	AU 9963259	A	20000515	AU 1999-63259	19991019
	AU 759275	B2	20030410		
	BR 9914638	A	20010703	BR 1999-14638	19991019
	EP 1123274	A1	20010816	EP 1999-950505	19991019
	EP 1123274	B1	20041229		
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	TR 200101126	T2	20010921	TR 2001-1126	19991019
	HU 2001003673	A2	20020228	HU 2001-3673	19991019
	HU 2001003673	A3	20030328		
	ZA 200101824	A	20020305	ZA 2001-1824	19991019
	EE 200100185	A	20020815	EE 2001-185	19991019
	EE 4849	B1	20070615		
	JP 2002528432	T	20020903	JP 2000-578279	19991019
	JP 3960754	B2	20070815		
	JP 2003246773	A	20030902	JP 2003-22576	19991019
	NZ 510098	A	20030926	NZ 1999-510098	19991019
	RU 2218328	C2	20031210	RU 2001-107853	19991019
	AT 286021	T	20050115	AT 1999-950505	19991019
	EP 1514867	A2	20050316	EP 2004-105861	19991019
	EP 1514867	A3	20050323		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, MK, CY, AL				
	PT 1123274	T	20050429	PT 1999-950505	19991019
	ES 2235522	T3	20050701	ES 1999-950505	19991019
	IN 2001CN00508	A	20050304	IN 2001-CN508	20010410
	US 20020032210	A1	20020314	US 2001-837166	20010419
	US 6706749	B2	20040316		
	NO 2001001956	A	20010420	NO 2001-1956	20010420
	KR 799892	B1	20080131	KR 2001-704970	20010420
	MX 2001PA04070	A	20010731	MX 2001-PA4070	20010423
	US 20020037905	A1	20020328	US 2001-923458	20010808
	US 6696475	B2	20040224		
	HK 1040699	A1	20061124	HK 2002-102082	20020319
PRAI	DK 1998-1362	A	19981022		
	DK 1997-452	A	19970422		
	WO 1998-DK162	W	19980421		
	US 1999-402165	A2	19990930		
	EP 1999-950505	A3	19991019		
	JP 2000-578279	A3	19991019		
	WO 1999-DK575	W	19991019		
	US 2001-837166	A2	20010419		

OS MARPAT 132:308142
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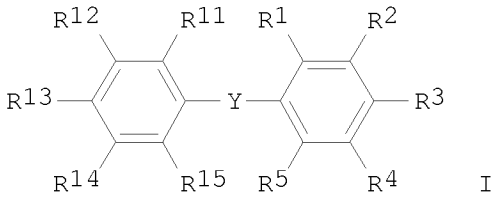

I

AB Title compds. [I; 1 of R1-R3 = acidic functional group having pKa<8 or a group convertible in vivo to such a group; R4, R5 and the others of R1-R3 = H, alkyl, alkoxy, OH, halo, CF3, cyano, NO2, amino, etc.; Y = C(:X)NR0, NR0C(:X)NR00, etc.; R0, R00 = H, alkyl; X = O, S; R11-R15 = H, alkyl, alkoxy, OH, halo, CF3, cyano, (substituted) aryl, heteroaryl, phenylamino, etc.], were prepared Thus, 3-trifluoromethylphenyl isocyanate and 2-aminobenzoic acid were stirred in PhMe to give N-3-trifluoromethylphenyl-N'-2-carboxyphenyl urea. N-3-trifluoromethylphenyl-N'-[4'-(dimethylsulfamoyl)-2-(1H-tetrazol-5-yl)-4-biphenyl]urea blocked erythrocyte chloride channels with KD = 0.3 μM.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT